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Evaluation of performance in some ultrasonic procedures for non-invasive thermal estimation into hyperthermia phantoms

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To dispose of a precise and non-invasive temperature measurement over the treated area becomes very important during hyperthermia treatments, in order to make possible an optimisation of their healing effects. A performance analysis of some previously reported ultrasonic techniques, which were proposed for non-invasive temperature estimation, is made in this work over simulated phantoms mimicking human tissues. A first technique is based on discrete scattering modelling for tissue characterization and spectral analysis of frequency distributions related to average scatters spacing [R. Seip & E.S. Ebbini]. Other technique uses certain relations between tissue temperature changes and time-shifts in echoes due to thermally induced sound velocity changes and expansions [R. Maass-Moreno & C.A. Damianou]. And finally, the third procedure analysed here, is a recently proposed alternative, based on phase demodulation processing, to estimate the indirect effects of echoes time-shifts in the phase domain [M. Vázquez, A. Ramos et al.]. The three options are analysed for the same multi-pulse echo patterns, looking for detecting possible advantages and inconveniences in each estimation case.

1. Generalities

There are a number of protocol driven techniques to induce internal temperatures under well-controlled conditions in hyperthermia treatments [1]. One of the most important parts in such a technique, is the thermometry system, because would permit to avoid strong deviations on the induced temperature distribution with regard to that ideally predicted (by feed-back correcting the emitting systems).

A fundamental aspect in this kind of systems is to provide, being comfortable for the patient, a real time accurate measure of temperature distribution in the irradiated tissues.

Pulsed ultrasound, at relatively high frequency, has a set of characteristics making this option well suited for temperature estimation inside a biologic tissue:

a) it provides a non-invasive measurement.
b) the good penetration of ultrasound at frequencies where the wavelengths are on the order of tenths of millimetre.
c) these small wavelengths allow the beams to be focused and properly controlled.
d) the feasibility of constructing ultrasonic transducers of virtually any shape and size.
e) it doesn't cause any toxic or ionising effect in the tissue.
f) compatibility with the type of ultrasonic transducers employed in the therapy.
e) and finally, its relative low cost.

The general objective of this work is to present an evaluation of performance, into hyperthermia phantoms, of some previously reported ultrasonic (US) techniques proposed for non-invasive temperature estimation. The aim is looking for detecting the possible advantages and the inconveniences in each optional technique.

2. Simulated Multipulse Echo Patterns

For this purpose, the irradiated tissue was considered as a semi-regular matrix of scatters separated by an average distance "*d*", as other authors suggest [2-8]. As a consequence, the whole received echo-trace, coming from this internal structure, could be considered as a sum of individual echoes from those scatters.
In this work, we will use a very limited modelling of the elemental echoes from the multiple reflectors, because we are only seeking to assess phenomena of thermal interest. In the numeric simulations of the behaviour of a tissue, and uniquely for our particular objective, we will make the approximations that the successive echoes preserve the form of the original pulse incident on tissue. Uniquely, their amplitudes will be attenuated by the tissue effect.
This means that not important dispersion with frequency in attenuation is supposed. In addition, punctual reflectors and far-field conditions will be considered, i.e., possible diffraction effects related to transducer aperture and/or to reflectors are assumed to be comparatively neglected [4].

In consequence, the ultrasonic pulse pattern representing an elementary echo coming from a punctual ideal reflector, could be simulated (in these conditions) by a simplified model $P(t)$, typical in this type of studies [5].

Resume of assumptions that were assumed:

- The successive echoes preserve the form of the pulse incident on tissue.
- Simulations were made in a temperature range from 25 to 44°C, but the analysis was focused mainly on real tissue temperature during a hyperthermia treatment: 35 to 42 °C.
- Temperature variations in steps of 1 °C.
- Radiation from an ultrasonic transducer of 2.25 MHz in central frequency.
- Echo amplitudes include attenuation from the travelled medium path, but not important dispersion with frequency.
- Punctual reflectors and far-field propagating conditions: i.e., the diffraction effects are neglected.
- Four punctual reflectors at transducer central axis (spaced by a distance d = 4 mm) are considered, and the received echo-signal is calculated by:

$$E(t) = \sum_{k=1}^{N} a_k P(t - (2x_k / c)) \qquad (1)$$

(x_k is the position of the reflector *k*, *c* is sound speed, and a_k is the amplitude of the echo "number *k*") [3].

Under these conditions, simulated patterns like that shown in Figure 1, are obtained.

3. Ultrasonic estimation of temperature

There are two principal important effects due to temperature rising in a tissue exposed to a hyperthermia treatment:

a) Ultrasound (US) velocity changes with T

b) Thermal expansion of the medium

These effects cause a time-shift on the ultrasonic echoes travelling through the tissue exposed to treatment.

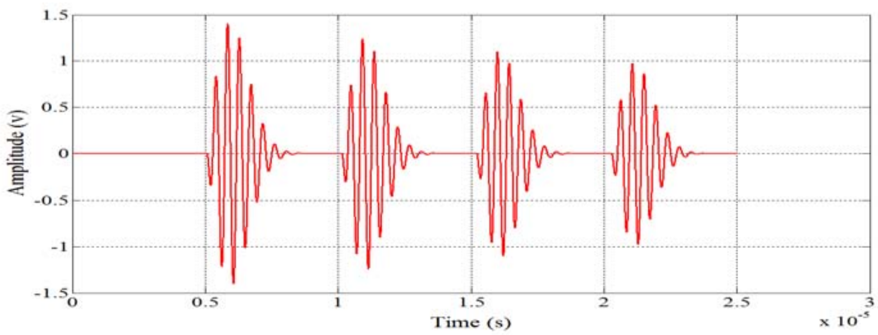

Figure 1. Calculated echo-trace with a central ultrasonic frequency of 2.25 MHz, and considering US pulses reflected from 4 punctual scatters spaced by 4mm.

3.1 Time delay analysis

In this type of time-delay analysis, the calculation of the delays between echoes employs (usually) a cross-correlation between signals taken at different temperatures [9-11]. Our simulated signal was divided in 4 windows in order to obtain (by applying cross-correlation) the delays-temperature variations for different phantom depths.

Defined windows have a length of 5 μs. The delays obtained in these windows for 19 distinct temperatures are shown in the Figure 2. A delay curve, focused on the real temperatures reached during hyperthermia treatment (calculated for one of these windows), and overlapped with quadratic and linear regressions for these data, are displayed on figure 3.

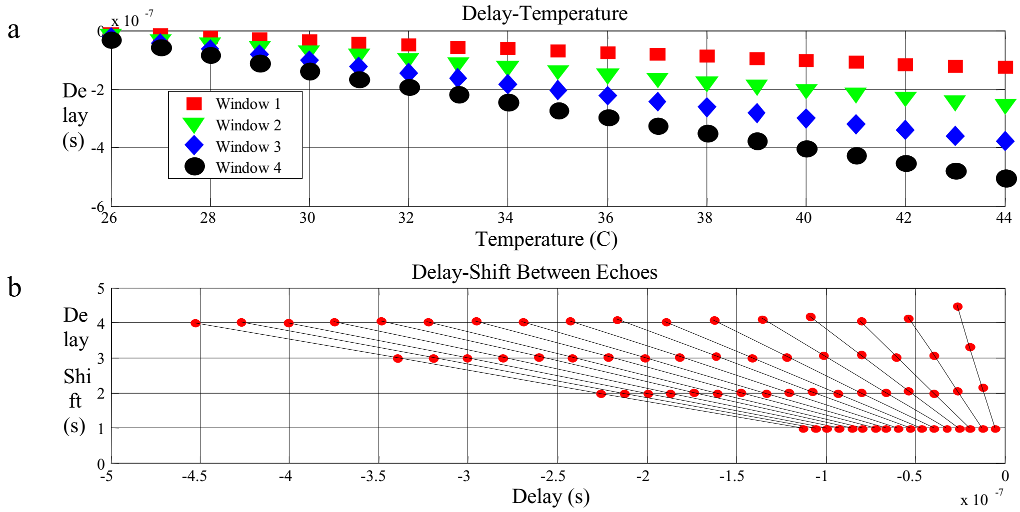

Figure 2. Delay-Temperature curves obtained for the four time-windows with a cross-correlation tool, applied to 19 ultrasonic signals simulated in a temperature range of 25°C to 44°C (using the signal at 25°C as reference one): a) Delay versus temperature; b) Delay versus delay shift percentage using the first delay of each window as unity.

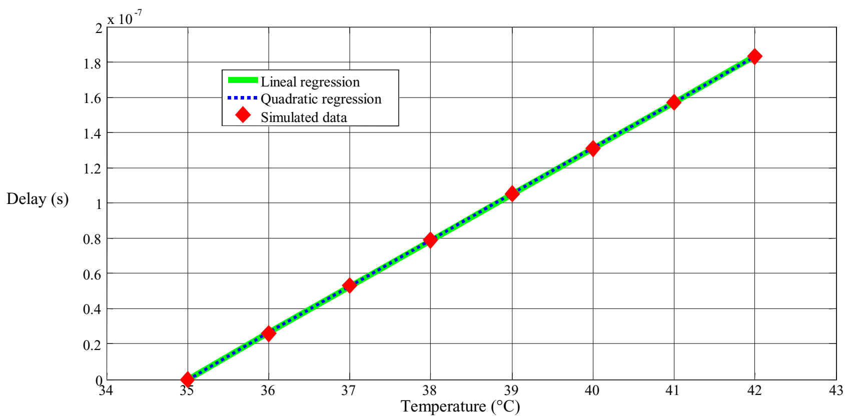

Figure 3. Delay-Temperature behaviour, in the time window number 1, as well as, quadratic and linear regressions in a temperature range from 35°C to 42°C (hyperthermia range).

3.2 Phase-Shift analysis

The measure of changes in the phase of the echo-signals with temperature is an indirect estimation of the delay [12,13]. In this study, a linear dependence of phase with temperature is obtained (see Figure 4) by using a demodulation method [12]. It can be appreciated a near to linear relation between phase and temperature values and also a very good resolution with temperature changes.

For the posterior analysis, the signal was divided in four windows too. Phase changes with temperature (35-42°C) were calculated at different phantom depths. Defined windows have a length of 3.5 µs approximately. Obtained phase shifts for one of these windows, and quadratic and linear regressions for these data are displayed on Figure 5.

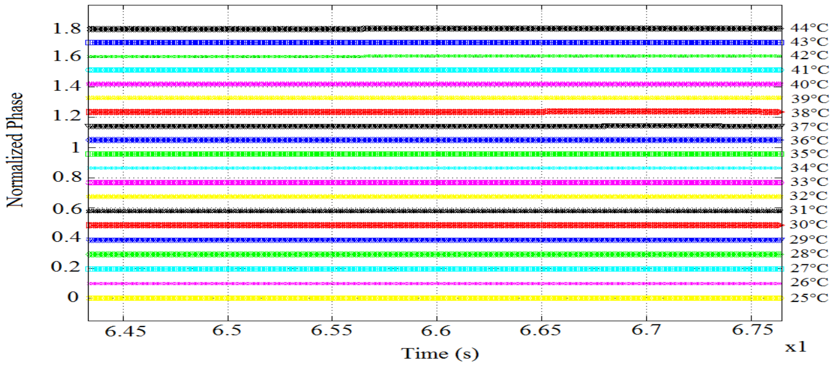

Figure 4. Phase curves resultant for simulated signals in a temperature range 25°-44°C. (zoom of the phases curves corresponding to the first echo in the reflected signal).

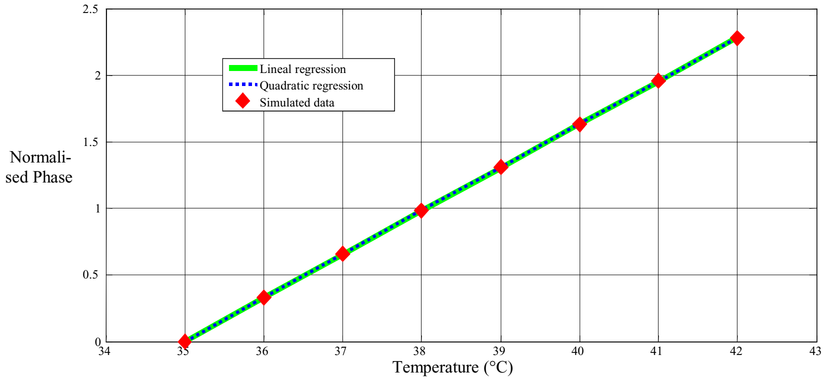

Figure 5. Phase-Shift versus temperature behavior in the time window 1, and quadratic and linear regressions.

3.3 Spectral analysis

Quantification of the shifts in the fundamental resonance frequency (and in its harmonic overtones), related to the averaged scatters distance [14], is used for temperature estimation, in this case. The signal was divided in two windows due to the calculation of fundamental frequency (f_1), related to a scattering uniform distribution, requires at least two echoes into the data windows, which have a length of 10.25 µs in this case. Frequency values for the 14th harmonic of f_1 in Power Spectrum Density (PSD) and quadratic & linear regressions for these data are displayed in the Figure 6, in a temperature range from 35 to 42°C.

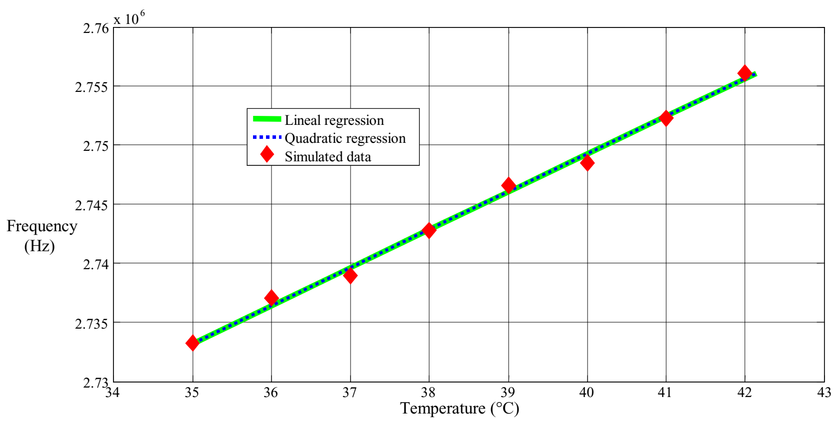

Figure 6. Frequency-Shift versus temperature and quadratic and linear regressions, in the time window 1.

4. Quadratic and linear regressions results calculated for the 3 estimation techniques

Quadratic and linear regressions coefficients, obtained for the established windows in each technique analysed here, are resumed on tables 1 and 2 respectively.
Regressions for relations [a) - T(d) and d(T), b) - T(p) and p(T), and c) - T(f) and f(T)] were calculated. Coefficients of the quadratic term (c'') in all the regressions of second order have a very small value in comparison with the other coefficients (c' and c), which confirms the linear behaviour observed in the data calculated for each technique.

	Window 4		Window 3		Window 2		Window 1	
	T(d)	d(T)	T(d)	d(T)	T(d)	d(T)	T(d)	d(T)
Time Shift Regression	$T=c4+c4'd+c4''d^2$	$d=c4+c4'T+c4''T^2$	$T=c3+c3'd+c3''d^2$	$d=c3+c3'T+c3''T^2$	$T=c2+c2'd+c2''d^2$	$d=c2+c2'T+c2''T^2$	$T=c1+c1'd+c1''d^2$	$d=c1+c1'T+c1''T^2$
c	3.50E+01	-9.85E-07	3.50E+01	-7.73E-07	3.50E+01	-5.05E-07	3.50E+01	-2.28E-07
c'	3.78E+07	2.98E-08	5.10E+07	2.42E-08	7.59E+07	1.55E-08	1.53E+08	6.50E-09
c''	2.68E+12	-4.76E-11	0.00E+00	-5.95E-11	0.00E+00	-2.98E-11	0.00E+00	0.00E+00
	T(p)	p(T)	T(p)	p(T)	T(p)	p(T)	T(p)	p(T)
Phase Change Regression	$T=c4+c4'p+c4''p^2$	$p=c4+c4'T+c4''T^2$	$T=c3+c3'p+c3''p^2$	$p=c3+c3'T+c3''T^2$	$T=c2+c2'p+c2''p^2$	$p=c2+c2'T+c2''T^2$	$T=c1+c1'p+c1''p^2$	$p=c1+c1'T+c1''T^2$
c	3.50E+01	-1.21E+01	3.50E+01	-8.89E+00	3.50E+01	-6.13E+00	3.50E+01	-3.11E+00
c'	3.04E+00	3.61E-01	4.07E+00	2.62E-01	6.06E+00	1.85E-01	1.21E+01	9.50E-02
c''	1.32E-02	-5.00E-04	1.58E-02	-2.00E-04	6.76E-02	-3.00E-04	3.26E-01	-2.00E-04
					T(f)	f(T)	T(f)	f(T)
Spectral Analysis Regression					$T=c2+c2'f+c2''f^2$	$f=c2+c2'T+c2''T^2$	$T=c1+c1'f+c1''f^2$	$f=c1+c1'T+c1''T^2$
c					0.00E+00	2.66E+06	0.00E+00	2.67E+06
c'					-3.00E-04	9.58E+02	-3.00E-04	5.79E+02
c''					1.08E-10	2.92E+01	1.08E-10	3.41E+01

Table 1. Quadratic regressions for different windows in simulated echo-signals, calculated for the three estimation techniques

	Window 4		Window 3		Window 2		Window 1	
Time Shift Regression	$T=l4+l4'd$	$d=l4+l4'T$	$T=l3+l3'd$	$d=l3+l3'T$	$T=l2+l2'd$	$d=l2+l2'T$	$T=l1+l1'd$	$d=l1+l1'T$
l	3.50E+01	-9.15E-07	3.50E+01	-6.85E-07	3.50E+01	-4.61E-07	3.50E+01	-2.28E-07
l'	3.83E+07	2.61E-08	5.10E+07	1.96E-08	7.59E+07	1.32E-08	1.53E+08	6.50E-09
Phase Change Regression	$T=l4+l4'p$	$p=l4+l4'T$	$T=l3+l3'p$	$p=l3+l3'T$	$T=l2+l2'p$	$p=l2+l2'T$	$T=l1+l1'p$	$p=l1+l1'T$
l	3.50E+01	-1.14E+01	3.50E+01	-8.54E+00	3.50E+01	-5.70E+00	3.50E+01	-2.85E+00
l'	3.07E+00	3.26E-01	4.09E+00	2.44E-01	6.14E+00	1.63E-01	1.23E+01	8.15E-02
Spectral Analysis Regression					$T=l2+l2'f$	$f=l2+l2'T$	$T=l1+l1'f$	$f=l1+l1'T$
l					-8.15E+02	2.62E+06	-8.15E+02	2.62E+06
l'					3.00E-04	3.20E+03	3.00E-04	3.20E+03

Table 2. Lineal regressions for the four windows, in simulated echo signals, calculated for the three estimation techniques

5. Discussion

Time correlation analysis was the option that presented less complexity because the used processing provided direct relation between time shift and temperature. This technique has a little sensibility to noise. Nevertheless its temperature resolution is affected by the fact that the time-shift values obtained are in the order of nanosecond/°C (1,1 ns/°C/mm), a very small step to detect, which requires a high sampling frequency and specific processing tools.

The Phase shift analysis overcomes this limitation since the step / °C is in the order of 0.08 rad., which represent a step easier to detect. Limitation of this technique concerns with its stability, and the signal has to be subjected to a delicate pre-processing to suppress possible oscillation due to external or coherent noises (before it can be processed by the phase-shift detection algorithm).

Finally, Spectral estimation analysis is a robust processing technique, capable to provide a very good temperature resolution; because the frequency step / °C is in the order of KHz / °C (3270 Hz / °C). With its use, the narrowband noise can be easily isolated. Its limitation is in the spatial resolution (because, at least two consecutive echoes has to be considered in each time window) and also in its sensibility to secondary frequency peaks in the PSD.

6. Conclusions

From the results of the 3 temperature estimation techniques (based on distinct ultrasonic analyses), when applied to simulated echo-signals, it can be concluded than all of them present advantages and limitations for the said estimation.

The three techniques require additional processing to improve their potential capabilities and the main limitations of each technique. It would be useful and interesting: a) to achieve a method by putting together the properties of these three techniques, thus suppressing local disadvantages in resolutions or processing time; and b) quantitatively evaluate the performance of these techniques for real biologic structures as phantoms and animal tissues.

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